

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

REC'D 16 NOV 2005

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference

96700/862

Date of mailing
(day/month/year)

14 NOV 2005

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/01773

International filing date (day/month/year)

23 January 2004 (23.01.2004)

Priority date (day/month/year)

24 January 2003 (24.01.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 49/00, 39/00, 39/02, 39/04; C12Q 1/00; C12P 1/00C12N 1/00 and US Cl.: 424/9.1, 9.2, 184.1, 234.1, 248.1;
435/4, 41, 243, 440, 253.1, 863

Applicant

ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Date of completion of this opinion
24 October 2005 (24.10.2005)

Authorized officer
Rodney P. Swartz, Ph.D.

Telephone No. 571-272-1600

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/01773

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ on paper
 - ☒ in electronic form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims 1-43 YES
Claims 44-86 NO

Inventive step (IS)

Claims 1-43 YES
Claims 44-86 NO

Industrial applicability (IA)

Claims 1-86 YES
Claims NONE NO

2. Citations and explanations:

Claims 1-86 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

Claims 45-86 lack novelty under PCT Article 33(2) as being anticipated by Mahairas et al (*Journal of Bacteriology*, Vol. 178, No. 5, pages 1274-1282, 1996).

The claims are drawn to the use of an attenuated mycobacterium for the manufacture of a medicament wherein said mycobacterium has two deletions.

Mahairas et al teach *M. bovis* BCG containing deletions of RD1 to RD3 and exhibiting attenuated virulence (Abstract; page 1274, paragraphs 2 and 3; Material and Methods section, pages 1275-1276; Figure 2; Figure 3; Discussion, pages 1281-1282).

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof:
Page 12, line 11, "animal" should be "animals",
Page 13, line 21, insert "a" between with and M.,
Page 14, line 19, "that is that does" should be "that does",
Page 43, line 29, "paranthesis" should be "parenthesis",

The drawings are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or content thereof:
Figure 1 does not display a label for "Panel a" as recited on page 14, line 25,
Figure 17 shows Panel A and Panel B, but the brief description does not recite these panels,
Figure 21 indicates two panels, but the brief description does not label these,
Figure 22, indicates panels "A-I", but the brief description recites "a-i",
Figure 23, indicates panels "A-E", but the brief description recites "a-e",
Figure 24, indicates panels "A-F", but the brief description recites "a-f",
Figure 25, indicates panels "A-E", but the brief description recites "a-f", the last panel does not appear to be labeled at all,

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-86 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 1-86 are indefinite for the following reason(s):

Claims 1 and 41 are recite "a method of treating a mammal", but does not recite what the treatment is for. Claims 2-40 and 42-43 depend from these claims but do not clarify the indefiniteness.

Claim 44 and 84 are directed to a use of a mycobacterium for manufacturing a medicament for treatment of a mammal, but does not recite what the treatment is for. Claims 45-83 and 83-86 depends from these claims but do not clarify the indefiniteness.

Claims 44-86 are drawn to the "use" of an attenuated mycobacterium for the manufacture of a medicament for treatment of a mammal. It is unclear what is meant by "use of". Does this mean that the attenuated mycobacterium is whole, broken up, or only certain parts of the cell are utilized/purified/isolated?

Claims 1-86 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because:

Claims 1-43 are drawn to a method of treating a mammal. Claims 44-86 are drawn to the use of a mycobacterium in the manufacture of a medicament for treatment of a mammal. Since the claims do not specify what the treatment is for, the entire scope of the claims are assessed. The instant disclosure only provides guidance/examples for treatment of mycobacterial infection, specifically, tuberculosis. The disclosure provides no guidance/examples for treatment of, e.g., cancer, mental illness, or other bacterial/viral diseases.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/01773

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 49/00, 39/00, 39/02, 39/04; C12Q 1/00; C12P 1/00C12N 1/00 US CL : 424/9.1, 9.2, 184.1, 234.1, 248.1; 435/4, 41, 243, 440, 253.1, 863 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 424/9.1, 9.2, 184.1, 234.1, 248.1; 435/4, 41, 243, 440, 253.1, 863 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) biosis caba caplus embase japio lifesci medline scisearch, sequence id search		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MAHAIRAS, G.G., et al. Molecular analysis of genetic difference between Mycobacterium bovis BCG and virulent M. bovis. March 1996, Journal of Bacteriology, Vol. 178, No. 5, pages 1274-1282, entire reference.	44-86
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 21 October 2005 (21.10.2005)		Date of mailing of the international search report 14 NOV 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Rodney P. Swartz, Ph.D. <i>Valerie Bell-Harris</i> Telephone No. 571-272-1600